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Journal of Clinical Psychopharmacology

The Anticonvulsant Lamotrigine in Treatment-Resistant Manic-Depressive Illness.

Journal of Clinical Psychopharmacology. 17(3):185-189, June 1997.

Sporn, Jonathan MD; Sachs, Gary MD

Abstract:

Anticonvulsants are used extensively in the treatment of bipolar disorder.Treating depression in bipolar disorder can be difficult because of the limited antidepressant effects of the standard mood stabilizers and the tendency of antidepressants to induce mania or decrease cycle length. Lamotrigine is a new anticonvulsant with few side effects that may have mood-stabilizing and elevating effects. Its mechanism of action probably involves the inhibition of excessive release of excitatory amino acids such as glutamate. Antiglutamatergic agents may be antidepressant and mood stabilizing. A case series of 16 patients treated with lamotrigine (dose range 50 mg to 250 mg, mean dose of responders = 141 mg) is presented along with two case reports. All patients were considered treatment-resistant bipolar type I or II. Patients were rated on average 5 weeks after starting lamotrigine using a semistructured follow-up form that included symptom rating, Clinical Global Impressions (CGI), and Global Assessment of Functioning (GAF) scores. Eight of 16 patients were rated as "responders" (CGI less or equal to 2) and had a mean increase of 16 in their GAF scores. Lamotrigine seems to have antidepressant and mood-stabilizing effects, but this requires confirmation in randomized, controlled trials. (J Clin Psychopharmacol 1997;17:185-189).

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Features

Alzheimer's or depression: Could it be both?

From MayoClinic.com
Special to CNN.com

Early **Alzheimer's** and **depression** share many symptoms, so it can be difficult even for doctors to distinguish between the two disorders. And, not surprisingly, many people with **Alzheimer's** also are depressed.

In fact, new studies have linked **depression** and **Alzheimer's**. People with a history of clinical **depression** also have an increased risk of eventually developing **Alzheimer's**.

Similar symptoms

In addition to sadness, **depression** causes loss of interest in once-enjoyable activities and hobbies. This also happens in **Alzheimer's**. Social and emotional withdrawal is common in both conditions, as are impaired memory and concentration.

As **Alzheimer's** disease progresses, communication skills break down. As a result, **depression** becomes even harder to recognize. Many people with moderate to severe **Alzheimer's** disease lack both the insight and the vocabulary to express how they feel or even to accurately answer direct questions about their symptoms.

BRAIN & NERVOUS SYSTEM

Degenerative Diseases

- Dementia: Not always **Alzheimer's**
- Communicating effectively with a person who has **Alzheimer's**
- Early-onset **Alzheimer's**: An interview with a Mayo Clinic specialist
- Early-onset **Alzheimer's**: Financial challenges
- **Alzheimer's** caregiving: Balancing your needs with those of your loved one
- **Alzheimer's** drugs: Real benefits despite limitations
- Diagnosing **Alzheimer's**: An interview with a Mayo Clinic specialist
- Caregiving: Maintain your support network
- **Alzheimer's**: Mementos help preserve memories

"For example," says Glenn Smith, Ph.D., a psychologist at Mayo Clinic, Rochester, Minn., "if you were to ask a person with **Alzheimer's** if he or she rested well last night, the response might be 'I'm OK,' even if that person had not slept at all."

An important distinction

Considering these difficulties, it's easy to see why some people with **depression** have been mistakenly diagnosed with **Alzheimer's**, and vice versa. The distinction is important, though. **Alzheimer's** has no cure, but people with **depression** — whether it accompanies **Alzheimer's** or not — usually respond quite well to treatment.

In fact, **depression** treatment dramatically improves the quality of life for people who have both **Alzheimer's** and **depression**. A thorough physical exam and psychological evaluation can help detect **depression** in people who have **Alzheimer's** disease.

Signposts for depression

To detect **depression** in people with **Alzheimer's** disease, doctors must rely more heavily on nonverbal cues than on self-reported symptoms. If a person with **Alzheimer's** displays one of the first two symptoms in this list, along with at least two of the others, he or she may be depressed.

- **Alzheimer's**: Smoothing the transition on moving day
- **Alzheimer's**: Spirituality can be comforting
- **Alzheimer's**: Dealing with daily challenges
- **Alzheimer's**: Dealing with family conflict
- Long-term care options for **Alzheimer's**
- **Alzheimer's**: Getting the most from medical appointments
- **Alzheimer's**: Managing sleep problems
- **Alzheimer's**: When driving becomes an issue
- **Alzheimer's** care: Practical tips
- Memory loss: When to seek help
- **Alzheimer's** or **depression**: Could it be both?
- **Alzheimer's**: Planning for the holidays
- **Alzheimer's**: How to help the caregivers
- Incontinence in **Alzheimer's** disease: What you can do
- **Alzheimer's**: Helping children understand the disease
- **Alzheimer's**: Making mealtimes easier
- Wandering: Understand and control it
- Exercise: A boost to physical and emotional well-being in people with **Alzheimer's**
- Mad cow FAQ: Don't panic — Get the facts

- Significantly depressed mood — sad, hopeless, discouraged, tearful
- Reduced pleasure in or response to social contacts and usual activities
- Social isolation or withdrawal
- Eating too much or too little
- Sleeping too much or too little
- Agitation or lethargy
- Irritability
- Fatigue or loss of energy
- Feelings of worthlessness, hopelessness or inappropriate guilt
- Recurrent thoughts of death or suicide

Men and women with **Alzheimer's** become depressed with equal frequency. This differs from the general population, in which women are more likely to experience **depression** than are men. People with **Alzheimer's** may also experience **depression** differently than do people without **Alzheimer's**. For example:

- Symptoms may be less severe.
- Episodes of **depression** may not last as long or recur as often.
- Talk of suicide and attempted suicide is usually less common.

Types of treatment

Support groups and professional counseling may help depressed people in the early stages of **Alzheimer's** disease, before their communication skills deteriorate. Increased mental stimulation and physical activity also may help alleviate **depression**.

Antidepressant medications are safe and effective, with minimal side effects. Physicians often try various drugs and dosages to see what works best for each individual. Results usually appear within just a few weeks.

Selective serotonin reuptake inhibitors (SSRIs) are the most common type of antidepressants used for people who also have **Alzheimer's**. These include citalopram (Celexa), sertraline (Zoloft), paroxetine (Paxil) and fluoxetine (Prozac).

People with **Alzheimer's** may also respond to antidepressants that inhibit the reuptake of brain chemicals other than serotonin. These include venlafaxine (Effexor), mirtazapine (Remeron) and bupropion (Wellbutrin).

Tricyclic antidepressants, such as nortriptyline (Pamelor) and desipramine (Norpramine), are no longer used as first-choice treatments. However, they may be prescribed if other medications aren't effective.

Some patients with **depression** and dementia may not respond to medication. Many of these patients benefit from electroconvulsive therapy (ECT).

- Electroconvulsive therapy: Dramatic relief for severe mental illness

Is depression a risk factor for Alzheimer's?

A recent study suggests **depression** in older people may precede the development of **Alzheimer's**. This seven-year study tracked both **depression** and **Alzheimer's** symptoms in hundreds of people age 65 or older.

No participants had **Alzheimer's** symptoms at the beginning of the study. But those who reported the most depressive symptoms on a yearly questionnaire they completed during the study were more likely to eventually develop **Alzheimer's**. In fact, this tendency grew stronger with each additional depressive symptom reported.

Further research is needed to explore this possible link and determine whether treating the **depression** can reduce the risk for subsequent **Alzheimer's**. For now, recognizing and treating **depression** in older people, regardless of whether they have **Alzheimer's** disease, remains the best bet.

- **Depression**

January 12, 2006

MayoClinic.com
Tools for healthier lives

Alzheimer's or depression: Could it be both?

Early Alzheimer's and depression share many symptoms, so it can be difficult even for doctors to distinguish between the two disorders. And, not surprisingly, many people with Alzheimer's also are depressed.

In fact, new studies have linked depression and Alzheimer's. People with a history of clinical depression also have an increased risk of eventually developing Alzheimer's.

Similar symptoms

In addition to sadness, depression causes loss of interest in once-enjoyable activities and hobbies. This also happens in Alzheimer's. Social and emotional withdrawal is common in both conditions, as are impaired memory and concentration.

As Alzheimer's disease progresses, communication skills break down. As a result, depression becomes even harder to recognize. Many people with moderate to severe Alzheimer's disease lack both the insight and the vocabulary to express how they feel or even to accurately answer direct questions about their symptoms.

"For example," says Glenn Smith, Ph.D., a psychologist at Mayo Clinic, Rochester, Minn., "if you were to ask a person with Alzheimer's if he or she rested well last night, the response might be 'I'm OK,' even if that person had not slept at all."

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In fact, depression treatment dramatically improves the quality of life for people who have both Alzheimer's and depression. A thorough physical exam and psychological evaluation can help detect depression in people who have Alzheimer's disease.

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fact, this tendency grew stronger with each additional depressive symptom reported.

Further research is needed to explore this possible link and determine whether treating the depression can reduce the risk for subsequent Alzheimer's. For now, recognizing and treating depression in older people, regardless of whether they have Alzheimer's disease, remains the best bet.

Coping with Coexisting Conditions

Unfortunately, as we age, we are at higher risk not only for **Alzheimer's** disease but also for **depression**, diabetes and high blood pressure. Any one of these conditions can prove difficult to manage, so what should you do if you're caring for someone who not only has **Alzheimer's** but also suffers from another coexisting condition?

Caring for someone with **Alzheimer**' disease who is otherwise healthy can be a challenge. But the situation can become much more complicated when the individual has another disabling condition as well. Many times the effects of a coexisting condition or its treatment regimen can induce increasing confusion and memory loss as well as unexpected behavioral changes in persons with **Alzheimer**' disease.

Because of the brain cell damage caused by **Alzheimer's**, affected individuals are often very vulnerable to developing side effects related to other conditions or the medicines prescribed for those conditions, says Constantine Lyketsos, MD, director of the Neuropsychiatry and Memory Group at Johns Hopkins Hospital in Baltimore, Maryland.

"Usually someone with **Alzheimer's** develops side effects more often and severely, and in an atypical way. For example, if a person is diabetic, he or she may exhibit confusion, sleep trouble, or agitation as a result of an imbalance in blood sugar level," he says. "These symptoms can exacerbate the confusion, sleep trouble, and agitation that already may be a result of **Alzheimer's**"

"Coexisting conditions, if not properly treated, can have a negative effect on individuals with dementia," adds Elizabeth Smith-Boivin, an administrator at the Millview Adult Home in Waterford, New York.

Start low and go high
The presence of another disabling condition makes it even more critical that caregivers monitor treatment of the person with **Alzheimer's**, says Jeffrey Cummings, MD, professor of neurology and director of the University of California, Los Angeles, **Alzheimer's** Disease Center. "Physicians also should realize that it is imperative to involve the caregiver in all therapeutic decisions."

Typically more than one physician is treating the person with **Alzheimer's**, especially when coexisting conditions occur. To avoid medication mishaps, the caregiver should inform each physician that the individual has **Alzheimer's** and state whether he or she is in the early, middle, or late stage of the disease. Armed with this knowledge, "The physician can consider these factors when prescribing medication and determining dosage for another condition," Lyketsos says.

If a person with **Alzheimer's** has more than one physician for different coexisting conditions, his or her

caregiver may want to designate one of the physicians as the *primary* physician. The caregiver should then keep the primary physician abreast of all other disabling conditions and treatments and the impact they are having on the individual, Smith-Boivin says. "Make sure at least one physician has all of the pieces of this complicated puzzle. Every bit of information should be shared so that the physician is well-equipped and can give the appropriate guidance," she says.

One way to minimize the side effects is to question the necessity of medicine for treating a condition, Lyketsos says. In cases where treatment is necessary, such as heart disease and diabetes, he suggests that the "caregiver find out the starting dosage and ask the doctor whether it can be halved."

Martin Farlow, MD, professor of neurology at Indiana University's Alzheimer's Disease Center in Indianapolis agrees: "You should start low in terms of dosage and frequently evaluate the effects of the medicines on the condition it is meant to treat and on the person's cognitive abilities."

The strategy for treating an individual with Alzheimer's who also suffers from a coexisting condition will vary depending on the situation. The following are some suggestions for minimizing the effects of three of the most common coexisting conditions: depression, diabetes, and high blood pressure.

Depression

Some signs of depression are similar to those of Alzheimer's, but physicians stress that Alzheimer symptoms are more progressive and include profound memory loss. Typical signs of depression are social withdrawal, confusion, sadness, irritability, and change in sleep patterns and appetite. Lyketsos estimates that 20-25 percent of people with Alzheimer's also suffer from depression. Many individuals with Alzheimer's become depressed because they are aware of losing their cognitive abilities.

Lyketsos recommends that activity-based therapy be tried first, particularly if the person has a case of mild depression. If a medication must be prescribed, caregivers might seek advice from a specialist--a geriatric psychiatrist or neurologist. The specialist will likely prescribe an antidepressant that might work best for someone with Alzheimer's disease, with fewer side effects.

Diabetes

In individuals who suffer from Alzheimer's and diabetes, medicines may not be causing the cognitive problems. Diabetic treatment taken orally is unlikely to cause side effects, Lyketsos says. But fluctuation in blood sugar level is likely the culprit behind worsening of cognitive abilities or behavioral changes, he says. Lyketsos recommends that caregivers monitor their loved one's sugar level more often during the day and, if necessary, consult with a physician to adjust medication accordingly.

High blood pressure

Persons with Alzheimer's with high blood pressure should avoid diuretics and antihypertensive drugs, which could cause memory deficit, disorientation, and behavioral problems, Farlow says. Another group of drugs used to treat high blood pressure, called ACE inhibitors, have minimal side effects and might be a better choice for individuals with dementia.

These suggestions are a starting point for discussions among the caregiver, individual with Alzheimer's, and physician to determine which options are available and which are best. When in doubt as to whether the treatment regimen prescribed is the best choice for someone with Alzheimer's, consult a physician for a thorough evaluation.

Health care professionals stress that keeping the person with Alzheimer's in general good health will lessen the effects of coexisting conditions or their treatments.

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Depression - elderly

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Depression among the elderly

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Depression is a medical illness characterized by persistent sadness, discouragement, and loss of self-worth. These feelings are accompanied by reduced energy and concentration, sleep problems (insomnia), decreased appetite and weight loss. In the elderly, it also frequently presents with excessive concerns about bodily aches and pains.

Causes, incidence, and risk factors *Return to top*

Detecting **depression** in the elderly may be complicated by several factors. Often the symptoms of **depression** such as fatigue, loss of appetite, and sleeping difficulties are associated with the aging process or a medical condition rather than with major depressive disorder.

Contributing factors include the loss of a spouse or close friends, chronic pain and illness, difficulty with mobility, frustration with memory loss, difficulty adapting to changing circumstances such as moving from a home to a retirement facility, or changes within the family.

Depression can also be a sign of a medical problem. It may be complicated by brain disorders associated with the aging process such as Alzheimer's disease.

Depression in the elderly is a widespread problem that is often not diagnosed and frequently undertreated. Many older individuals will not admit to signs and symptoms of **depression** for fear of being seen as weak or crazy.

Symptoms *Return to top*

- depressed or irritable mood
- feelings of worthlessness or sadness
- loss of interest or pleasure in daily activities
- temper, agitation
- change in appetite, usually a loss of appetite
- change in weight
    - unintentional weight loss (most frequent)
    - weight gain
- difficulty sleeping
    - daytime sleepiness
    - difficulty falling asleep (initial insomnia)
    - multiple awakenings through the night (middle insomnia)
    - early morning awakening (terminal insomnia)
- fatigue (tiredness or weariness)
- difficulty concentrating
- memory loss
- abnormal thoughts, excessive or inappropriate guilt
- excessively irresponsible behavior pattern
- abnormal thoughts about death
- thoughts about suicide
- plans to commit suicide or actual suicide attempts

If these symptoms are present every day for more than 2 weeks, then **depression** is likely present.

Signs and tests *Return to top*

- a physical examination will help determine if there is a medical illness causing the **depression**
- psychological evaluation
- blood tests: CBC or blood differential, thyroid function tests, liver or kidney function tests
- a variety of other tests may be indicated

Treatment *Return to top*

Sometimes **depression** can be alleviated by social interventions to help with isolation or loneliness such as group outings, volunteer work for the healthy elderly, or regular visits from concerned people.

Treatment of underlying medical conditions or the discontinuation of certain medications may alleviate symptoms.

Antidepressant drug therapy has been shown to increase quality of life in depressed elderly patients. These medications are carefully monitored for side effects, and doses are usually lower and increased more slowly than in younger adults.

Neuroleptic medications may help treat agitation in some individuals. Electroconvulsive therapy (ECT) may be indicated in the severely depressed if other measures are unsuccessful.

Expectations (prognosis) *Return to top*

If detected, **depression** may respond to medical treatment. Undetected, it may lead to complications. The outcome is usually worse for those who have limited access to social services, or to family or friends who can help promote an interest in activities.

Complications *Return to top*

Depression may be complicated by Alzheimer's disease or other forms of dementia. It may also complicate other medical conditions in the elderly. Untreated **depression** in the elderly is associated with a high rate of suicide.

Calling your health care provider *Return to top*

Call your health care provider if you are feeling worthless or hopeless or if you are crying frequently. Also call if you feel that you are having difficulty coping with stresses in your life and want a referral for counseling.

Go to the nearest emergency room or call your local emergency number (such as 911) if you are having thoughts of suicide or of taking your own life.

If you are caring for an aging family member and think they might be suffering from **depression**, contact their health care provider. Often, older patients will not admit to signs and symptoms of **depression** out of pride.

Prevention *Return to top*

Prevention is related to the contributing factors. Social supports that help deal with losses, mobility changes, and so on can be helpful. In many cases, there is no effective prevention.

Update Date: 11/10/2003

Updated by: Vineeth John, M.D., Department of Psychiatry, University of Pittsburgh Medical Center, Pittsburgh, PA. Review provided by VeriMed Healthcare Network.